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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/825,068	04/14/2004	Chih-Ping Liu	55600-8014.US03	7994

22918 7590 10/17/2006

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EXAMINER	
HISSONG, BRUCE D	
ART UNIT	**PAPER NUMBER**
1646	

DATE MAILED: 10/17/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/825,068	LIU ET AL.	
	Examiner	Art Unit	
	Bruce D. Hissong, Ph.D.	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 July 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,4,6,8,10 and 11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3, 4, 6, 8, 10, 11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/26/06, 7/24/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Formal Matters

1. Applicants' response to the office action mailed on 4/24/2006, including arguments/remarks, and amendments to the specification and claims, was received on 7/24/2006 and has been entered into the record.

2. Claims 2, 5, 7, 9, and 12-14 were cancelled in the amendment received on 7/24/2006. Therefore, claims 1, 3-4, 6, 8, and 10-11 are currently pending and are the subject of this office action.

3. The text of those sections of Title 35, U.S.C. not included in this action can be found cited in full, in the previous office action mailed on 4/24/2006.

Priority

Applicants' amendments to the specification to remove a claim to the benefit of co-pending U.S. Application No. 09/910,406, to U.S. Provisional Application No. 60/219,128, and to Japanese Application No. 317160, is noted. Therefore, as set forth on page 3 of the office action mailed on 4/24/2006, the earliest effective filing date of the instant application is 3/10/2004.

Information Disclosure Statement

1. The information disclosure statement received on 4/26/2006 has been considered by the Examiner. Citation 49 has been lined through because publication date is not listed. A full citation for this reference appears on the accompanying PTO form 892.

2. The information disclosure statement received on 7/24/2006 has been fully considered by the Examiner.

Claim Rejections - 35 USC § 112, second paragraph

Rejections withdrawn

Rejection of claims 1, 3-4, 6, 8, and 10-11 under 35 USC § 112, second paragraph, as being incomplete for omitting a conclusion step for the method of increasing the IL-10/IL-12 blood ratio in a subject, as set forth on page 3 of the prior office action mailed on 4/24/2006, is *withdrawn* in response to Applicants' amendments to the claim to include a conclusion step that recites continuing to orally administer IFN-τ to the subject....."to maintain the increase in IL-10/IL-12 blood ratio."

Claim Rejections - 35 USC § 112, first paragraph - enablement

Rejections withdrawn

Rejection of claims 1, 3-4, 6, 8, and 10-11 under 35 USC § 112, first paragraph, regarding lack of enablement for a method of increasing the IL-10/IL-12 blood ratio in a subject suffering from an autoimmune disorder, or a method for inhibiting progression of an autoimmune disorder, wherein said autoimmune disorder is any autoimmune disorder other than multiple sclerosis, as set forth on pages 5-6 of the prior office action mailed on 4/24/2006, is withdrawn in response to Applicant's amendments to independent claims 1 and 8 to recite a method of increasing the IL-10/IL-12 blood ratio in a human subject suffering from multiple sclerosis (claim 1), or a method of inhibiting progression of multiple sclerosis in a human subject.

Rejections maintained

Claims 1, 3-4, 6, 8, and 10-11 *remain rejected* under 35 USC § 112, first paragraph, regarding lack of enablement for methods of increasing the IL-10/IL-12 blood ratio, or inhibiting progression of autoimmune disease, by administration of any IFN-τ other than the polypeptides defined by SEQ ID NOs 2 or 3, as set forth on pages 4-5 of the prior office action mailed on

4/24/2006. In the response received on 7/24/2006, the Applicants amended claims 1 and 8 to recite administration of IFN-τ, wherein said IFN-τ protein "has a sequence having 80% sequence identity to SEQ ID NO: 2", and assert that the specification is enabling for the claims as currently amended.

This argument has been fully considered and is not found persuasive. As amended, the breadth of the claims is still excessive because the claims are drawn to administration of any protein that is at least 80% identical to the polypeptide of SEQ ID NO: 2. The specification provides guidance and examples showing administration of the polypeptides defined by SEQ ID NOs 2 and 3, and is therefore enabling for methods using these polypeptides. However, the specification does not teach or provide examples of any protein that is less than 100% identical to the polypeptide of SEQ ID NO: 2, and provides no evidence showing that a protein with less than 100% homology to SEQ ID NO: 2, when administered to a human suffering from multiple sclerosis, would increase the IL-10/IL-12 blood ratio and/or inhibit disease progression. Furthermore, the specification lacks guidance or examples that should show a person of ordinary skill in the art how to make, and then use, any polypeptide that is less than 100% identical to SEQ ID NO: 2 or 3 in a manner that is commensurate in scope with the claims. A skilled artisan would not be able to predict which amino acid residues, or regions of the polypeptide of SEQ ID NO: 2 could be modified by addition, deletion, or substitution, and still result in a polypeptide that is capable of increasing the blood IL-10/IL-12 ratio or inhibiting disease progression in patients suffering from multiple sclerosis.

In summary, the claims as currently amended are still excessively broad because they are drawn to administration of any polypeptide that is at least 80% identical to SEQ ID NO: 2. The specification does not provide guidance or examples showing how to make and then use any polypeptide with less than 100 homology to SEQ ID NO: 2, and a person of ordinary skill in the art would therefore require further, undue experimentation to make and then use any polypeptide, other than those of SEQ ID NOs 2 or 3, that is capable of increasing the IL-10/IL-12 blood ratio, or inhibiting disease progression in a subject suffering from multiple sclerosis.

Claim Rejections - 35 USC § 112, first paragraph – written description

Rejections maintained

Claims 1, 3-4, 6, 8, and 10-11 *remain rejected* under 35 USC § 112, first paragraph, regarding lack of written description for method of administering IFN-τ polypeptides with less than 100% identity to the proteins of SEQ ID NOs 2 or 3, as set forth on pages 6-7 of the prior office action mailed on 4/24/2006. In the response received on 7/24/2006, the Applicants amended claims 1 and 8 to recite administration of IFN-τ, wherein said IFN-τ protein "has a sequence having 80% sequence identity to SEQ ID NO: 2", and assert that the specification provides adequate written description for such polypeptides.

This argument has been fully considered and has not been found persuasive. As stated in the above enablement rejection, the amended claims are drawn to administration of any polypeptide that is at least 80% identical to the polypeptide of SEQ ID NO: 2. The specification does not describe any polypeptide that is less than 100% identical to the IFN-τ polypeptides of SEQ ID NOs 2 or 3. The instant specification also does not describe any regions or residues of SEQ ID NO: 2, or SEQ ID NO: 3, that can be modified and produce an IFN-τ polypeptide that can be used in a manner commensurate in scope with the claims. Therefore, the specification does not provide adequate written description for the genus of IFN-τ polypeptides recited by the claims as currently amended.

Claim Rejections - 35 USC § 103

Rejections maintained

Claims 1, 3-4, 6, 8, and 10-11 *remain rejected* under 35 USC § 103(a) as being obvious over the combination of Soos *et al*, in view of van Boxel-Dezaire *et al*, and further in view of Petereit *et al*, as set forth on pages 7-8 of the prior office action mailed on 4/24/2006. In summary, Soos teaches treatment of multiple sclerosis by oral administration of an IFN-τ polypeptide that is 100% identical to the sequence of SEQ ID NO: 2, and teaches that oral administration of IFN-τ increases serum IL-10 levels, but is silent regarding administration of IFN-τ at a dose of 5×10^8 units/day. van Boxel-Dezaire discloses that multiple sclerosis is

characterized by decreased IL-10 levels and increased IL-12p40 levels, and Petereit shows that multiple sclerosis patients with low IL-10 secretion had higher disability scores.

In the response received on 7/24/2006, the Applicants argue that the combined teachings of Soos *et al*, van Boxel-Dezaire *et al* and Petereit *et al* does not teach every limitation set forth in the claims. Specifically, the Applicants assert that the combined references fail to teach a method of increasing the IL-10/IL-12 ratio by oral administration of IFN-τ at a dose of 5×10^8 units/day. Furthermore, the Applicants also argue that the combined references do not provide an expectation of success in administering IFN-τ at 5×10^8 units/day.

These arguments have been fully considered and are not found persuasive. The teachings of Soos *et al* would motivate a person of ordinary skill in the art to treat patients suffering from multiple sclerosis by oral administration of IFN-τ. Soos *et al* discloses a molecule effective in treating multiple sclerosis (IFN-τ), an effective route of administration (oral), and benefits of this treatment regime (increased IL-10 levels). The teachings of Petereit *et al* and van Boxel-Dezaire *et al* provide further motivation to practice a method of treating multiple sclerosis that increases IL-10 levels in the treated patient. Regarding the claimed dosage of IFN-τ, while Soos *et al* does not explicitly teach oral administration of IFN-τ at 5×10^8 units/day, there is nothing in the disclosure of Soos *et al* that teaches away from this dosage. Soos *et al* shows that IFN-τ administration favorably treats multiple sclerosis and increases IL-10 serum levels. Thus, the showing by the Applicants that a higher dosage of IFN-τ also increases IL-10 levels would not be an unexpected result. The Applicants contend that the data shown in Figures 1A and 1D of the instant application would indicate that the doses disclosed by Soos *et al* may not be effective to increase IL-10 blood levels. However, it is noted that the 3 IFN-τ dosages taught in Figures 1A and 1D (2×10^7 U/day, 8×10^7 U/day, and 1.8×10^8 U/day) do not induce IL-10 levels that are statistically significantly different (see page 38, paragraph 0142), and there is no disclosed correlation between these induced IL-10 levels and the prognosis of the patients. Thus, there is nothing in the instant disclosure that would indicate that levels of IL-10 induced by 5×10^8 U/day of IFN-τ would be unexpectedly higher than the levels induced by IFN-τ at $2 \times 10^7 - 1.8 \times 10^8$ U/day, which fall within the range taught by Soos *et al* (see page 5, line 12 of Soos *et al*).

Finally, although the teachings of Soos *et al*, van Boxel-Dezaire *et al*, and Petereit *et al* do not explicitly disclose an increase in the IL-10/IL-12 blood ratio, it would be expected, in the absence of evidence to the contrary, that the IFN-τ-mediated increase in IL-10, as taught by

Soos *et al*, would inherently increase the IL-10/IL-12 blood ratio in multiple sclerosis patients receiving IFN-τ therapy.

Double Patenting

Rejections withdrawn

1. Provisional rejection of claims 1, 3-4, 6, 8, and 10-11 on the grounds of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 and 5-11 of co-pending Application No. 10/994,653, as set forth on pages 9-10 of the prior office action mailed on 4/24/2006, is *withdrawn* in response to the Applicants' arguments methods of increasing the IL-10/IL-12 ratio in multiple sclerosis is not obvious over promoting weight loss in an individual.

2. Provisional rejection of claims 1, 3-4, 6, 8, and 10-11 on the grounds of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-5 of co-pending Application No. 10/346,269, as set forth on pages 9-10 of the prior office action mailed on 4/24/2006, is *withdrawn* in response to the Applicants' arguments that the claims of the instant application do not recite a patient population in a fasted state.

3. Provisional rejection of claims 1, 3-4, 6, 8, and 10-11 on the grounds of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-4 of co-pending Application No. 10/719,472, as set forth on pages 9-10 of the prior office action mailed on 4/24/2006, is *withdrawn* in response to the Applicants' arguments that measuring OAS levels in a patient is not obvious over measuring the IL-10/IL-12 ratio in a patient.

Rejections maintained

4. Claims 1, 3-4, 6, 8, and 10-11 *remain provisionally rejected* on the grounds of nonstatutory obviousness-type double patenting as being unpatentable over co-pending Application Nos. 10/825,382, 10/825,457, 10/824,710, 11/040,706, and 10/884,741, as set forth on pages 9-10 of the prior office action mailed on 4/24/2006. The Applicants' terminal disclaimer filed for these applications has been noted and made of record. Pending acceptance

of said terminal disclaimer, the claims remain rejected. Upon approval of said terminal disclaimer, the rejection will be withdrawn.

5. Claims 1, 3-4, 6, 8, and 10-11 *remain provisionally rejected* over claims 1, 17, and 18 of co-pending Application No. 11/112,369, as set forth on pages 9-10 of the prior office action mailed on 4/24/2006. In the response received on 7/24/2006, the Applicants argue that the claims of the '369 application are drawn to methods of identifying a human subject having an IL-10 deficiency and administering IFN-τ in an amount effective to increase blood IL-10 levels, and that because the instant claims do not recite "identifying a subject having an IL-10 deficiency", the instant application is not an obvious variant of the '369 application. These arguments have been fully considered and are not found persuasive. It is known in the art that multiple sclerosis patients exhibit decreased levels of IL-10 secretion (see Soos et al, above). Thus, a skilled artisan would know that identifying a multiple sclerosis patient would inherently identify a patient with an IL-10 deficiency, and therefore the '369 application is an obvious variant of the instant application.

Conclusion

No claim is allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bruce D. Hissong, Ph.D., whose telephone number is (571) 272-3324. The examiner can normally be reached M-F from 8:30 am - 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, Ph.D., can be reached at (571) 272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

BDH
Art Unit 1646

ROBERT S. LANDSMAN, PH.D
PRIMARY EXAMINER